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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/611,835	07/07/2000	Brent R. Stockwell	50164/002002	6924

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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
LUNDGREN, JEFFREY S	
ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
11/05/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	09/611,835	STOCKWELL ET AL.	
	Examiner	Art Unit	
	JEFFREY S. LUNDGREN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *89-156* is/are pending in the application.

4a) Of the above claim(s) *89-153* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *154-156* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DEATAILED ACTION

Reassignment of Application

Please note that this application has been reassigned to Examiner Jeffrey Lundgren, in Art Unit 1639. In order to expedite accurate processing of the application papers, all future correspondence with the Office should reflect this change.

Status of the Claims

Following the Decision on Appeal from the Board of Patent Appeals and Interferences (BPAI) on April 20, 2007, Appellants filed a Request for Rehearing on June 25, 2007, requesting reconsideration of the rejection of claims 89-156 as unpatentable over Stylli, West, Burgin and Chiang.

In response, BPAI issued a Decision on Rehearing on November 20, 2007, reaffirming the rejection of claims 89-153 over Stylli, West, Burgin and Chiang, but withdrew the rejection over claims 154-156.

Claims 89-156 are pending in the instant application; because the rejection of claims 89-153 has been affirmed by BPAI, these claims are withdrawn from consideration; claims 154-156 are the subject of the Office Action below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 154-156 are obvious in view of Edwards and Edwards:

Claims 154-156 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Edwards, U.S. Patent No. 5,885,782, issued on March 23, 1999, in view of Lam *et al.*, U.S. Patent No. 5,510,240, issued on April 23, 1996.

The claims are directed towards a method of screening a library of compounds for a given activity in living cells that corresponds to a potential therapeutic use. Compounds from the library that have been identified as "active" are then tested in various combinations with at least one other active compound from the library to determine if there is, for example, a synergistic effect.

Specifically, claim 154 is drawn to a method for discovering a desired two or higher order combination of compounds having the ability to affect a biological property of living cells in a way that is indicative of the potential for therapeutic efficacy in an animal, said method comprising the steps of:

(a) contacting living test cells with at least 100 compounds under conditions that ensure that each compound/test cell contacting is segregated from the others,

(b) detecting or measuring a biological property of said test cells,

(c) selecting compounds that cause a change in said biological property relative to said biological property of said test cells not contacted with said compounds,

(d) contacting at least 49 unique two or higher order combinations of the selected compounds of step (c) with living test cells under conditions that ensure that each; contacting is segregated from the others,

(e) detecting or measuring a biological property of said test cells of step (d), and

(f) identifying combinations of compounds that cause an effect on said biological property of said test cells that is different from the effect of each compound of the combination by itself, wherein said identified combinations of compounds have potential therapeutic use in an animal.

Edwards is directed towards methods for identifying compounds/compositions that inhibit the growth of microorganisms, in particular, fungi. Edwards summarizes the focus of his disclosure in the following statement:

> The compositions consist of chemically-synthesized antibiotics comprising certain amino acids. Methods of identifying particular antibiotic compositions from libraries of such compositions are disclosed. In addition, methods for preventing microbial growth in plants and animals are disclosed. Methods and compositions are also disclosed which relate to synergistic combinations of inhibitory peptides with other antimicrobial compounds.

Edwards, Abstract.

As in steps (a)-(c) of claim 154, Edwards teaches a first step of creating a library of peptide compounds, and screening the compounds for activity, for example, antifungal activity which can be used as antifungal therapeutics:

> A method of treating a fungal disease is also disclosed. The method comprises ***first creating a synthetic peptide combinatorial library*** and ***contacting aliquots of the synthetic peptide combinatorial library with a cell*** of a fungus believed to be the causative agent of the disease. Next, a process of ***selecting those aliquots of the synthetic peptide combinatorial library which most reduce the growth of the fungal cell*** is carried out.

Edwards, col. 9, lines 1-8. The peptide library suggested by Edwards comprise at least 100 compounds, such as the suggested 400 peptide compound compositions (col. 6, line 23-25).

As in steps (d)-(f), Edwards further teaches using the selected peptides in combination, specifically, as two or higher order combinations, and testing for synergetic properties:

> For purposes of this invention, ***a synergistic combination or composition between a peptide or an aliquot of a peptide library occurs when two or more compounds distinct from the peptide or peptide library aliquot are observed to be more inhibitory to the growth of a test organism than the individual components alone***. Specifically, as will be described in detail below, one calculates the expected additive inhibition of the combination by summing the known inhibition levels of each component. ***The combination is then tested on the test organism to derive an observed additive inhibition. If the observed additive inhibition is greater than that of the expected additive inhibition, synergy is exhibited***. While the examples to follow utilize non-peptides such as nystatin, fluconazole, miconazole, and amphotericin B to generate synergistic combinations with the antifungal peptides of the invention, ***it will be understood by those of***

> ***skill in the art that the same sorts of tests can be applied to find synergism between two or more antimicrobial peptides or peptide library aliquots***. Similarly, while the examples are limited to two component mixtures, ***the methods of the invention can equally well be utilized with mixtures of more than two components so long as the individual inhibition levels are known for each such component.***
>
> The methods of the invention utilized to detect synergistic combinations comprises first creating a synthetic peptide combinatorial library. As in previous tests, each aliquot of the library represents an equimolar mixture of peptides in which at least the two C-terminal amino acid residues are known. Using the tests described above, it is possible to determine for each such aliquot of the synthetic peptide combinatorial library, precisely calculated concentration at which it will inhibit a test organism.
>
> The next step in the general methods of the invention used to detect synergy involves mixing the aliquot of the synthetic peptide combinatorial library with at least one antimicrobial compound to create a test mixture. ***As with the peptide component of the mixture, the antimicrobial compound must be one having a known ability to inhibit a test organism. Next the methods of the invention call for contacting said test organism with the test mixture, and measuring the inhibition of growth of said the test organism as compared to at least one untreated control***. More controls are desirable, such as a control for each individual component of the mixture. Similarly, where there are more than two components being tested, the number of controls to be used must be increased in a manner well known to those of skill in the art of growth inhibition testing. ***After the growth inhibition studies are complete, it is possible to determine an expected additive effect and an observed additive effect on the inhibition of growth. These two values are then compared to determine whether a synergistic inhibition of growth of said test organism has occurred***.

Edwards, col. 11, line 19 to col. 12, line 3 (emphasis added).

As in claim 155, Edwards suggests that the test cells of the individual library members are the same as the test cells combination of library members:

> As with the peptide component of the mixture, the antimicrobial compound must be one having a known ability to inhibit a test organism. ***Next the methods of the invention call for contacting said test organism with the test mixture***, and measuring the inhibition of growth of said the test organism as compared to at least one untreated control.

Edwards, col. 11, lines 54-60 (emphasis added).

As in claim 156, Edwards teaches that the biological property tested using the individual library members is the same as the combination of library members:

> ***As with the peptide component of the mixture, the antimicrobial compound must be one having a known ability to inhibit a test organism***. Next the methods of the invention call for contacting said test organism with the test mixture, and measuring ***the inhibition of growth of said the test organism as compared to at least one untreated control***.

Edwards, col. 11, lines 54-60 (emphasis added).

Although Edwards teaches synthesizing and screening large starting peptide libraries for antifungal activity, followed by the aforementioned synergy screening procedure with a number of peptide combinations, Edwards does not explicitly teach "*at least 49* unique two or higher order combinations of the selected compounds of step (c)" in the disclosed synergy screen.

Lam is directed towards, among other aspects of the disclosure, methods for screening large libraries of oligopeptides for identifying compounds having the desired activity. Lam teaches a method where a large synthetic random library of oligopeptides having a variable pentapeptide segment are prepared on beads and screened (2,476,099 oligopeptides), and happens to result in 75 beads yielding positive activity results – see col. 37, line 25 to col. 38, line 34, including Table 1.

One or ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because each of Edwards and Lam are directed towards the screening libraries of oligopeptide compounds in order to identify member compounds having the desired activities. Although the activity of the compound libraries studied in each of Edwards and Lam are different, the combined teachings suggest that the number of library members for a starting library are known (*e.g.*, if not for at least the reason that Edwards already states 400 compound compositions). Similarly, one of ordinary skill in the art would also conclude based on the number of active compounds identified from the initial library of each Edwards and Lam, that "at least 49" unique two or more higher order combinations to be a suggested value for performing a synergy screening as taught by Edwards. For example, in addition to Lam's 75 compounds identified as active, see Edwards' working examples that result in the identification of numerous oligopeptides having antifungal activity that are then used with multiple antibiotic compounds having antifungal activity – *i.e.*, results in Tables X and XIV-

XXVIII. The number of active compounds identified in both references, and the suggested synergy strategy of Edwards that teaches making combinations of active compounds from the identifying step, one or ordinary skill in the art would recognize "at least 49" as a number of combinations to draw from in creating the "synergy library." Moreover, Applicants' specific claim to the numerical limitations of the library size for individual screening and synergy screening is comparable to the size of compounds first screened individually and in combination. See *Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device. Furthermore, there is no information of record, by way of Applicants' original disclosure, a declaration submitted by Applicants' nor art record, that would suggest that the claimed library size of "at least 49" results in improved/unexpected performance beyond the library sizes in either Edwards or Lam, for Edwards' synergy assays. Therefore, the invention as whole was *prima facie* obvious at the time it was invented.

Common Ownership of Claimed Invention Presumed

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. §§ 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Conclusions

No claim is allowable.

If Applicants should amendment the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should

point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (*e.g.*, if the amendment is not supported *in ipsis verbis*, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeff Lundgren whose telephone number is 571-272-5541. The Examiner can normally be reached from 7:00 AM to 5:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christopher Low, can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey S. Lundgren
Patent Examiner, Art Unit 1639

/Christopher S. F. Low/
Acting Director of Technology Center 1600